In the Sequence Listing :

Please replace the sequence listing submitted on October 29, 2001 with the substitute sequence listing submitted herewith.

In the Figures:

Please replace originally-filed Figures 1-13 with the substitute Figures 1-13 submitted herewith.

REMARKS

Specification

The substituted paragraphs on pages 33, 37, 76, 107, and 108 were amended merely to add SEQ ID NOs in compliance with 37 CFR § 1.821 (d). Marked-up versions of each of these paragraphs are submitted in Appendix A.

The substituted paragraph on page 59 was amended merely to delete a typographical error. A marked-up version of the paragraph is submitted in Appendix A.

No new matter has been added by way of these amendments to the specification.

Sequence Listing:

The sequence listing has been amended to include the sequences of SEQ ID NOs: 58-62, which sequences are found in the originally-filed specification at pages 33, 37, 76, 107 and 108, respectively. No new matter has been added by way of the amendment to the sequence listing.

In compliance with 37 C.F.R §§ 1.821-1.825 and § 1.52(e), the applicants herewith submit the Sequence Listing in written form and computer readable form (3.5 inch disk). The

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written form and computer readable forms of the Sequence Listing are identical. A statement under 37 CFR § 1.821(f) is submitted herewith.

The Sequence Listing has been generated from the specification and does not constitute new subject matter. The Sequence Listing has been prepared with PatentIn Ver.2.0 and checked with Checker Version 3.0 Program. No error has been found.

Figures

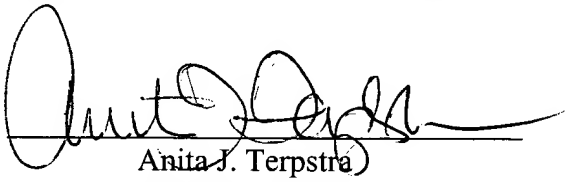
Substitute Figures 1-13 are submitted as formal drawings. Figure 13 was amended merely to include the SEQ ID NO of the sequence shown in the figure in compliance with 37 CFR § 1.821(d). The substitute Figures 1-13 and a marked-up version of the originally-filed Figure 13 are attached as Appendix B. No new matter has been added by way of this amendment.

Conclusion

If the Examiner has any questions regarding the amendments submitted herewith, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Date: December 18, 2002

By: 
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Appendix A

(Marked-up copy of the specification amendments)

Page 33, first paragraph:

includes an additional 180 nucleotides at the 5' end corresponding to the following 60 amino-terminal amino acids: MACWPQLRLLLWKNLTFRRRQTCQLLLEVAWPLFIFLILISVRLSYPPYEQHECH FPNKA **(SEQ ID NO. 58)**. Given that there is an in-frame stop codon 6 to 9 nucleotides upstream from this location, the newly predicted start site is the first methionine codon that could produce a continuous open reading frame. Alignment of this new ABC1 cDNA sequence with related ABC transporter sequences ABCR and ABC-C (also known as ABC3) which also contain open reading frames for the 60 additional amino acids, indicates a high degree of similarity, implying that the homologous ABC transporter proteins begin with sequences related to the amino terminal extension sequence proposed for human ABC1. It is likely that the earlier published start site of the human ABC1 was predicted from the published mouse ABC1 cDNA sequence (Luciani et al., *Genomics,* 21150-159 (1994); GenBank Accession no.: X75926) which contains an extra nucleotide "n" in the extension region such that the newly disclosed methionine is not in-frame. However, if the "n" nucleotide in the mouse sequence is ignored, the mouse and human sequences of the extension region are identical. In light of these results, it is likely that the full length human ABC1 protein contains 2261 amino acids rather than 2201 amino acids, as previously suggested by Langmann et al. and others. Accordingly, Langmann et al. do not present the full open reading frame of human ABC1.

Page 37, first paragraph:

sequences. For example, the full length 3' UTR (SEQ ID NO: 6) contains 46 sequences (AA)nCU/UC(AA)n **(SEQ ID NO: 59)** which have been shown to be necessary for binding of Vigilin. Vigilin, a ubiquitous protein with 14K homology domains, is the estrogen-inducible vitellogenin mRNA 3'-untranslated region binding

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protein (*J. Biol. Chem.*, 272: 12249-12252 (1997)). In addition to binding HDL, Vigilin has been shown to bind to the 3' flanking region of mRNAs and to increase the half-life of the mRNA transcript (*Mol. Cell. Biol.*, 18:3991-4003 (1998)). Thus, the 3' flanking region could be altered, for example, to increase the binding of Vigilin, thereby increasing the half-life of the ABC1 mRNA. Preferably, the isolated polynucleotide comprises the sequence shown in SEQ ID NO: 4. Also preferably, the isolated polynucleotide comprises the sequence shown in SEQ ID NO: 5. In another preferred embodiment, the isolated polynucleotide comprises the sequence shown in SEQ ID NO: 6. In other preferred embodiments, the polynucleotide comprises a sequence that hybridizes, under stringent conditions, to the nucleotide sequence set forth in SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

Page 59, first paragraph:

therapeutic effect. A typical dosage may range from about 0.1 [?]g/kg to about 100 mg/kg or more, depending on the factors mentioned above.

Page 76, third paragraph:

The amount of ABC1 protein can be assayed using any of the well-known methods of measuring protein. Preferably, the amount of ABC1 protein is measured using an immunoassay. In one embodiment, the amount of ABC1 protein is determined by (a) contacting the cell sample with a population of anti-ABC1 antibodies and (b) detecting the anti-ABC1 antibodies associated with the cell sample. For example, the ABC1 protein can be contacted with an antiserum raised against a synthetic peptide corresponding to KNQTVVDAVLTSFLQDEKVKES **(SEQ ID NO. 60)** located at the C-terminus, as described in Example 11. The anti-ABC1 antibodies can be detected using several methods known in the art, including, for example, western blotting, immunoprecipitation, and FACS, wherein the detection can be accomplished using

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radioactive, colorometric, or fluorescent labeling. One preferred method for measuring the amount of ABC1 protein in a cell sample is immunoprecipitation, wherein biotinylated ABC1 proteins are contacted with anti-ABC1 antibody and the bound anti-ABC1 antibody is detected using streptavidin horse radish peroxidase.

Page 107, fourth paragraph:

To determine which portion of the 5' flanking region of ABC1 retains transcriptional activity in response to nuclear ligands, various plasmids containing a different portion of the 5' flanking region and a luciferase reporter gene were transfected into RAW 264.7 cells treated with at least one ligand for the nuclear receptors. Using this system, an sterol response element corresponding to nucleotides 1480-1510 of SEQ ID NO: 3 was identified. The sterol response element contains a direct repeat-4 element TGACCGatagTAACCT **(SEQ ID NO: 61)**. Confirmation of the sterol response element was obtained using site-directed mutagenesis and band-shift assay techniques.

Page 108, third paragraph:

Site-Directed Mutagenesis: The sterol response element corresponding to nucleotides 1480-1510 of SEQ ID NO: 3 was mutated in the 1080-1643 sequence described above using site-directed mutagenesis. Specifically, the response element containing a direct repeat-4 element TGACCGatagTAACCT **(SEQ ID NO: 61)** was mutated to CTGCACatagTAACCT **(SEQ ID NO: 62)** using the GeneEditor system (Promega, Madison, WI) according to the manufacturer's protocol.

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